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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,625	04/04/2006	Tine Hoff	10355.204-US	9296
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EXAMINER VOGEL, NANCY TREPTOW				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/574,625

Applicant(s)

HOFF, TINE

Examiner

NANCY VOGEL

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-44 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 23-44 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/55/08)
Paper No(s)/Mail Date 4/4/06
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____

DETAILED ACTION

Claims 23-44 are pending in the case.

Receipt of the Information Disclosure Statement on 4/4/06 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-28, 32-34, 38, 39, 43, 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41

USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

A written description of an invention involving a chemical genus, like a description of a chemical species, "requires a precise definition, such as by structure, formula, [or] chemical name," of the claimed subject matter sufficient to distinguish it from other materials. *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not a sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*,

the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include: (1) Actual reduction to practice, (2) Disclosure of drawings or structural chemical formulas, (3) Sufficient relevant identifying characteristics (such as: i. Complete structure, ii. Partial structure, iii. Physical and/or chemical properties, iv. Functional characteristics when coupled with a known or disclosed, and correlation between function and structure), (4) Method of making the claimed invention, (5) Level of skill and knowledge in the art, and (6) Predictability in the art.

"Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a genus of methods using a secretion stress inducible promoter, or using a secretion stress inducible promoter which is in its normal position linked to a gene encoding a polypeptide which has at least 70% or 80% identity to the amino acid sequence of SEQ ID NO:2.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 23-28, 32-34, 38, 39, 43, 44 are broad and generic, with

respect to all possible promoters and cells. The possible structural variations are numerous since they encompass methods using any secretion stress inducible promoter, or any promoter which normally is linked to a gene encoding any protein which has at least 70% or 80% identity to SEQ ID NO:2. Specifically, the claims lack written description because one could not predict the structure of a promoter which has the recited property. Therefore, one of ordinary skill in the art would not be able to determine which promoter would have the recited property without trial and error experimentation, and thus the structure-function correlation is considered to be unpredictable. Regarding the claims drawn to promoters normally linked to a protein having 70 or 80% identity to SEQ ID NO:2, there is no structural information recited regarding the promoter itself, and regarding the protein structure, the specification does not provide sufficient descriptive support for the myriad of proteins encompassed by the claims, and the specification does not provide a representative number of examples of promoters normally linked to protein encoding regions having the recited identity to SEQ ID NO:2. such that one of ordinary skill in the art would be able to envision the next species of the genus of polypeptides and promoters that have the recited activity.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide

adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29, 35, 40, rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29, 35, and 40 are vague and indefinite in the recitation of "comprised by". It is not clear what this term is intended to mean. It is noted that there are other claims drawn to the same subject matter, but with the transitional phrase "comprises" (claims 30, 36, and 41), it is not clear if the claims 29, 35, and 40 are intended to encompass different metes and bounds that rejected claims 29, 35, and 40.

Claims 25, 26 are vague and indefinite in the recitation of "wherein the regulator protein controls the expression of the reporter gene", or "wherein the regulator protein is an activator or repressor of the expression of the reporter protein". Since claim 24 recites that either a gene encoding a reporter or a regulator protein is present, it is not clear what is intended by claims 25 and 26, which appear to recite that both the reporter and regulator are present.

Claim 37 is vague and indefinite in the recitation that "the promoter is identical to the octameric motif of SEQ ID NO:3", since it is disclosed in a reference referred to in the specification (page 9, Darmon et al.) that the sequence of SEQ ID NO:3 is the -35 region of the promoter, but promoters are known to comprise a -35 and a -10 region. Therefore it is unclear how the octamer of SEQ ID NO:3 can be considered a promoter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23-28, 39, 43, 44 are rejected under 35 U.S.C. 102(a) as being anticipated by Griffith et al. (FASEB Journal, 17, No. 4-5, 2003, Abst. No. 369.8) (cited by applicants) or Griffith et al. (FEBS LETT. 2003, 553(1-2), pp. 45-50) (cited by applicants).

Griffith et al. (FASEB J) or Griffith et al. (FEBS Lett.) disclose host cells where the activity of the unfolded protein response (UPR) is monitored using a UPR element-lacZ fusion. This response is considered equivalent to "secretion stress". Griffith et al. (FASEB J) discloses "different copy numbers of an integrating TeP2 vector". Different

copy numbers of the same gene can be considered a gene library. (see abstract of Griffith et al. (FASEB J.) , see page 47, col. 2 of Griffith et al. (FEBS Lett.)).

Claims 23-28, 39, 43 and 44 are, rejected under 35 U.S.C. 102(b) as being anticipated by Jones et al. (Embo J. 16, 6394-6406, 1997).

Jones et al. discloses activation of a degP-lacZ reporter upon overproduction of either PapE or PapG. Page 6399 column 2 last paragraph, further states that "The presence of misfolded or partially denatured proteins in the periplasm is thought to be a signal that leads to activation of degP transcription". In fact degP is also known as htrA-, i.e. one of the genes, the promoter of which is proposed to be used for monitoring of secretion stress in the present application. In any case, the reference discloses expression of several genes (i.e. a library) in a host where the activity of a promoter responsive to secretion stress can be monitored.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 29-38, 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lesley et al. (Protein Eng. 2002, 15:153-160) or Waldo (Curr Opin Chem Biol

2003, 7:33-38) in view of Noone et al. (J. Bacteriol. 183,b 2, 2001, 654-663) (all cited by applicants).

Lesley et al. or Waldo each teach the strategy of monitoring a host cell's response to protein overproduction by testing the activity of stress promoters. Many stress promoters (e.g. promoters of the heat shock response) respond to the presence of unfolded proteins in a cell, including unfolded proteins generated using overexpression strategies. IN order to monitor such stress induced by unfolded proteins. a reporter gene is typically expressed under the control of e.g. a heat shock promoter. Clones (or growth conditions) that allow expression of a target protein without triggering the stress response can then be selected. The instant application differs from Lesley et al. or Waldo in that secreted proteins are concerned. However Noone et al disclose the secretion stress promoter disclosed in the instant claims. It would have been obvious to one of ordinary skill in the art to have substituted the promoter disclosed by Noone et al. in the methods disclosed by Lesley et al. or Waldo, since all of the references disclose promoters operatively linked to reporter genes, that response to environmental conditions of stress induced by expression of particular types of proteins. One would have been motivated to do so by the desire to screen for secreted proteins, which is known to be useful for ease of production and purification of the protein produced. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

NV
3/1/09